Acetylenes

AC24

AC26

AC26 AC15 AC19

AC16

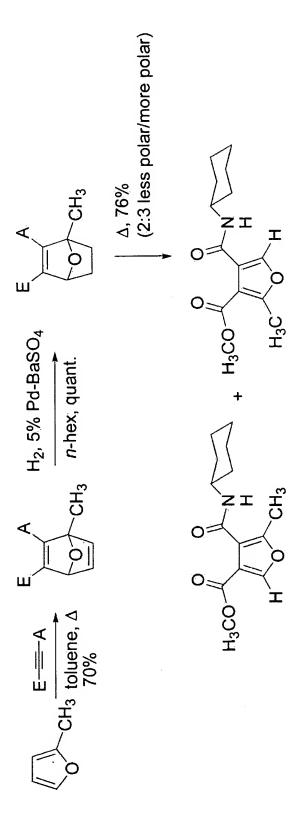
AC16

AC19

AC19

AC19 ACT ACT AC3
AC4
AC5 K1P

### Development of planar scaffold molecules



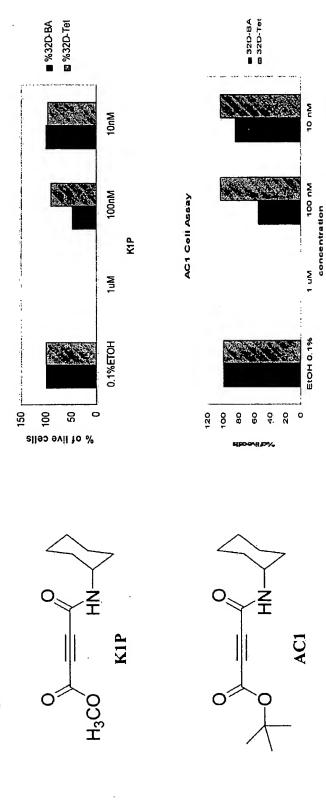
## Development of planar scaffold molecules, 2

#### FIGURE 4

#### Library of Acetylenes

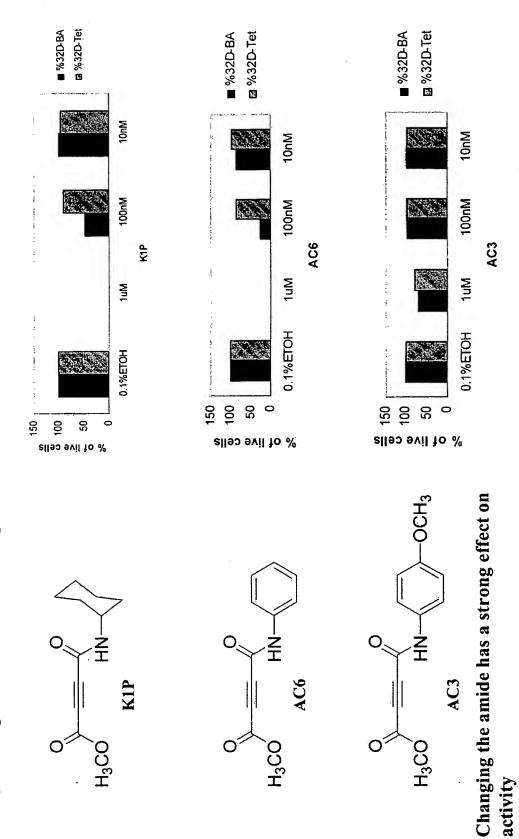
$$\begin{array}{c|c}
O & = & H & i) \text{ n-BuLi, THF, -78°C} & O & O \\
\hline
R_1O & & R_1O & R_2
\end{array}$$

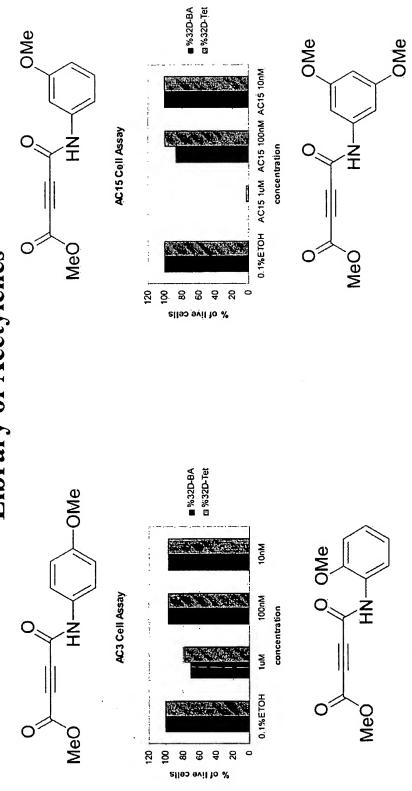
### 1) Investigation of the scaffold left side

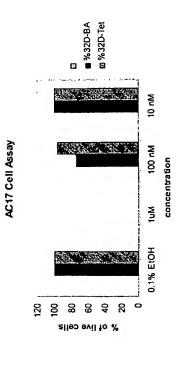


Both molecules exhibited similar activity, despite difference at the ester moiety; optimisation continued with modifications at the amide site

### 2) Investigation of the scaffold right side







■ %32D-BA

AC16 Cell Assay

8 8 8

10 nM

100 nM

S S

0.1% EtOH

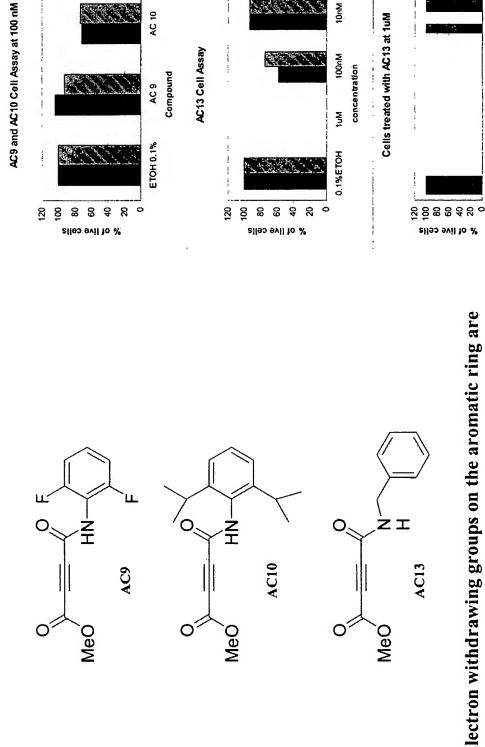
<del>2</del> 8 0

% of live cells

concentration

■ 32d BA %

m 32D-Tet%



□ %32D-Tet

10nM

■ %32D-BA

■%32D-BA ■ %32D-Tet

000,01

2000

1900

1000

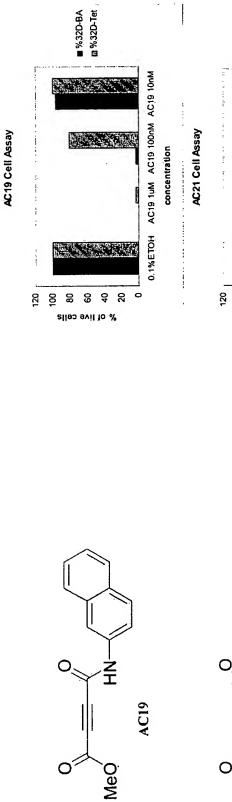
900

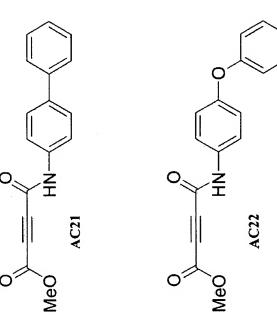
200

0.1%ETOH

cell number per well

- · Electron withdrawing groups on the aromatic ring are detrimental to activity
- Steric hindrance at the o-position has little effect on activity
- · Phenyl group on the amide can be replaced by a benzyl group





■ % 32D-BA ■ % 32D-Tet

8 6 6 8

% of cell growth

8

10 nM

100 nM

Ž

0.1% EIOH

concentration

AC22 Cell Assay

5 5 8 8 8 8 8

% of cell growth

AC21 and AC22 have lost selectivity displayed by AC19 but not the activity

■ %32D-BA B %32D-Tet

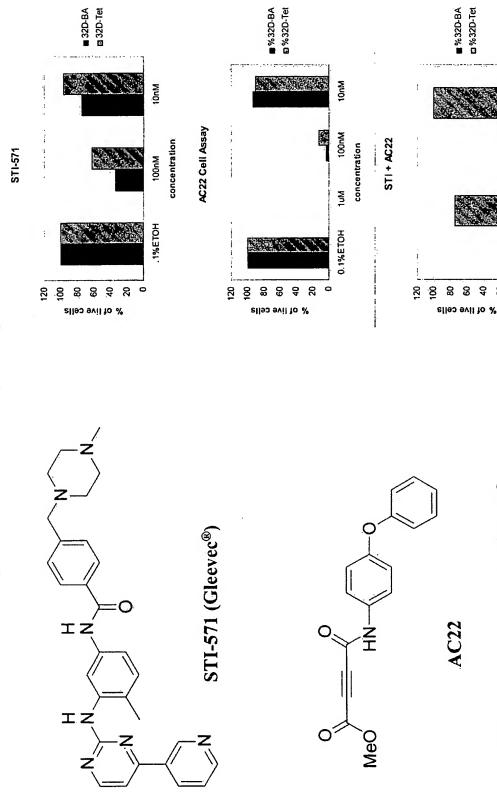
100nM

<u>Σ</u>

0.1%ETOH

concentration

## Some acetylenes exhibit synergism with STI-571



10.nM

100 nM

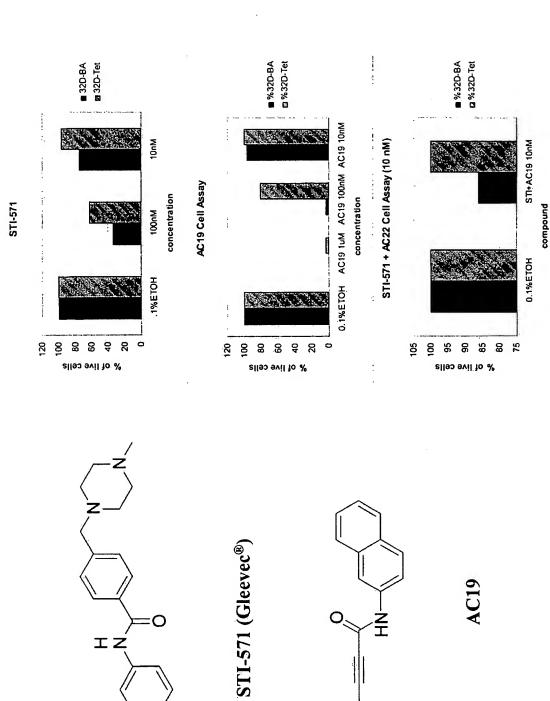
9

8

AC22 works in synergy with Gleevec®

concentration

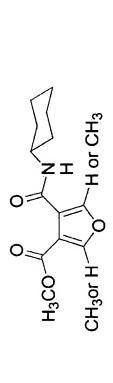
ΙŹ



MeO

# Testing of one furan from the second generation furan library

Recently, furans containing a H and a CH<sub>3</sub> were tested and proved to be active





cell inhibition assay of AN7BP